In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: October 13, 2015

JEREMIAH MEANS,	*	**PUBLISHED**
	*	No. 12-740V
Petitioner,	*	
v.	*	Chief Special Master Dorsey
	*	
SECRETARY OF HEALTH	*	Entitlement; Tetanus Diphtheria and
AND HUMAN SERVICES,	*	acellular-Pertussis ("Tdap") vaccine;
	*	Influenza ("flu") vaccine;
Respondent.	*	Susac's Syndrome;
	*	Significant Aggravation.

Donald P. Edwards, Law Office of Donald P. Edwards, Atlanta, GA, for petitioner.
Glenn A. MacLeod, United States Department of Justice, Washington, DC, for respondent.

RULING ON ENTITLEMENT[1]

I. INTRODUCTION

On November 1, 2012, Jeremiah Means ("petitioner" or "Mr. Means") filed a petition for compensation under the National Vaccine Injury Compensation program ("the Program")[2] alleging that as a result of receiving an influenza ("flu") vaccination on November 6, 2009, and a tetanus, diphtheria, and acellular-pertussis ("Tdap") vaccination on November 7, 2009, he suffered hearing loss, generalized weakness, and gait instability. Petition at ¶¶ 1, 7. Petitioner later developed his claim to allege that the vaccinations at issue significantly aggravated his

[1] Because this published ruling contains a reasoned explanation for the action in this case, the undersigned intends to post this decision on the website of the United States Court of Federal Claims, in accordance with the E-Government Act of 2002 § 205, 116 Stat. 2899, 2913 (Dec. 17, 2002) (codified as amended at 44 U.S.C. § 3501 (2014)). In accordance with the Vaccine Rules, each party has 14 days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Further, consistent with the rule requirement, a motion for redaction must include a proposed redacted ruling. If, upon review, the undersigned agrees that the identified material fits within the requirements of that provision, such material will be deleted from public access.

[2] The Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§ 300aa-10 et seq. Hereafter, individual section references will be to 42 U.S.C. § 300aa.

Susac's Syndrome; or alternatively, that the vaccinations caused him to suffer an encephalopathy as described in the Vaccine Injury Table ("Table")[3]. See Petitioner ("Pet'r") Prehearing Submission at 1; Pet'r Posthearing Brief at 1. Respondent recommends against compensation, stating petitioner has not met his burden of showing that the vaccinations at issue significantly aggravated his Susac's Syndrome. Respondent ("Resp't") Posthearing Brief at 26. Respondent further argues that the evidence does not demonstrate that petitioner suffered a Table encephalopathy; or alternatively, respondent argues that the weight of the evidence shows petitioner's alleged encephalopathy was caused by his Susac's Syndrome, a factor unrelated to the vaccines. Id. at 17, 24.

The parties filed expert reports in support of their respective positions. Petitioner filed two reports from his treating neuro-immunologist, Dr. John Rinker. See Exhibit ("Ex.") 9, 16-2. Respondent filed a report from a neuro-immunologist, Dr. Subramaniam Sriram. See Ex. A. An entitlement hearing was held on December 17, 2014, where Mr. Means and his wife, Ashley Means, testified. Dr. Rinker testified as an expert witness on behalf of petitioner, and Dr. Sriram testified as an expert for respondent. Additionally, both parties filed respective prehearing submissions, a joint prehearing submission, and posthearing briefs.

The parties agree that petitioner received two covered vaccines, flu and Tdap, and agree that petitioner experienced headache symptoms prior to receipt of the vaccines. Amended ("Am.") Joint ("J.") Prehearing Submission ("Sub.") at 1-2. They also agree that petitioner was correctly diagnosed with Susac's Syndrome and that he suffered residual effects or complications of his alleged vaccine injury for more than six months. Id. at 2. At the hearing, petitioner further argued that the Tdap vaccine caused him to suffer a Table encephalopathy within seventy-two hours of vaccination. Tr. at 108-114. He provided testimony from Dr. Rinker in support of this claim and respondent provided testimony from Dr. Sriram in rebuttal. Therefore, the issues to be decided are whether petitioner's Susac's Syndrome was significantly aggravated by his flu vaccination, Tdap vaccination, or a combination thereof; and whether as a result of receiving a Tdap vaccination petitioner suffered a Table encephalopathy within the requisite time period.

Based on a review of the entire record, the undersigned finds by preponderant evidence that petitioner suffered a significant aggravation of Susac's Syndrome under Loving v. Sec'y of Health & Human Servs., 86 Fed. Cl. 135 (2009). Accordingly, petitioner is entitled to compensation on the significant aggravation claim. Because the undersigned finds that petitioner is entitled to compensation, a decision or ruling on the issue of the Table claim is not reached.

[3] A "Table" injury is an injury listed on the Vaccine Injury Table, 42 C.F.R. § 100.3, corresponding to the vaccine received within the specified time frame.

II. BACKGROUND

A. Summary of Relevant Facts[4]

Mr. Means was twenty-four years old when he received a flu vaccination on November 6, 2009, and a Tdap vaccination on November 7, 2009. Petition at ¶ 2. Prior to his vaccinations, Mr. Means had an unremarkable medical history and lived an active lifestyle. Id. at ¶ 7. He received the vaccines while participating in a monthly drill exercise with the United States Air Force Reserve ("Air Force"). Hearing Transcript ("Tr.") at 9-11. As a reserve flight medic, Mr. Means regularly engaged in physical activity, as his job required carrying and loading heavy medical equipment onto military planes to care for those on board. Tr. 64-65. In the weeks prior to his vaccinations, Mr. Means underwent physical training in hopes of becoming an active duty Air Force SERE[5] specialist. Tr. 21-22; 73-74. When not working in the reserve, he was employed full time as an emergency medical technician at St. Francis Hospital in Columbus, Georgia. Tr. 61.

Concerning the events leading up to vaccination, Mrs. Means testified that on the afternoon of Sunday, November 1, 2009, petitioner and his father repaired the roof of a shed by placing plywood underneath a tin covering. Tr. 12-13, 83. Petitioner testified that he did not wear sunglasses while he worked, and as a result developed a "twinge of a headache." Tr. 83. Mrs. Means recalled her husband complaining of a headache later that Sunday and remembers reprimanding him for causing his own headache by not wearing sunglasses. Tr. 13.

According to Mr. and Mrs. Means, Mr. Means' headache resolved after several days and was gone prior to his vaccinations on November 6 and 7, 2009. Specifically, when the undersigned asked whether petitioner experienced a headache on Wednesday, November 4, 2009—the day he arrived at Maxwell Air Force Base for his monthly drill exercise—Mr. Means testified that he did not. Tr. 88. When asked whether he had a headache on Thursday, November 5, 2009, he replied that he did not. Tr. 89-90. Further, Mr. Means testified that he received the flu vaccine on Friday, November 6, 2009, and that he did not experience a headache on that day. Tr. 91. Mrs. Means testified that her husband did not complain of a headache until the following Sunday, November 8, 2009, after his vaccinations. Tr. 11-12.

On Saturday, November 7, 2009, Mr. Means received the Tdap vaccine. Ex. 1 at 1. Although he could not recall the exact time of day he received it, he estimated that he must have been vaccinated in the morning, as he remembered being told "to go back to the clinic and get another vaccine" when he arrived for drill that day. Tr. 91.

Petitioner testified that he began to experience a headache sometime after his vaccination

[4] This Summary of Facts section only contains a review of the most relevant facts, although the undersigned has considered the record as a whole in reaching her decision in this ruling. A more detailed recitation of the facts may be found in Respondent's Rule 4 report and in the parties' respective prehearing and posthearing briefs.

[5] SERE is an acronym for Survival, Evasion, Resistance, and Escape specialty training. Tr. 73-74.

on Saturday, November 7, 2009, and that it progressively worsened into the morning of Sunday, November 8, 2009. Tr. 92 -93. Petitioner characterized the headache as unlike what he had experienced the week before. Petitioner testified that he felt pressure at the base of his head which "felt like [he] was in a pool and [that he] was drowning." Tr. 84. At some point on Sunday, this pressure became "more of [a] stabbing sensation," that would not "go away." Tr. 94-95. On the drive back home to Columbus, Georgia, the Sunday evening after drill, petitioner experienced a severe headache and the onset of "flashes of firecracker light." Tr. 12; see also Ex. 2 at 37.

The contemporaneous medical records reflect that on Monday afternoon, November 9, 2009, petitioner visited his primary care physician, Dr. Terry Cone, complaining of a "headache, since Sunday." Ex. 2 at 37. Dr. Cone noted that petitioner felt as though his head would "explode" when he bent down below his chest. Id. Dr. Cone also noted petitioner's complaints of photophobia and blurring vision. Id. He ordered an MRI of the brain, which was performed on that Monday evening at an outpatient radiology center. Id. at 13. Petitioner was accompanied by his wife to obtain the MRI. Tr. 48-49. Mrs. Means testified that in the moments leading up to the scan, petitioner was "really restless and irritable," "agitated" and behaved uncharacteristically. Tr. 48-49. She further testified that he complained about "how much the sound and the light in the MRI [bothered] him." Tr. 48. Petitioner testified that "every sound was hurting his head," and as a result he had a difficult time lying still. Tr. 98-99. The MRI report noted that part of his study was "technically unreadable because of motion and/or artifact or both." Ex. 2 at 13. Otherwise, the study was unremarkable and revealed normal results. Id.

At 7:00 p.m. Monday evening, November 9, 2009, petitioner went to work a twelve hour shift in the emergency department ("ED") at St. Francis Hospital. He testified that while at work, his colleagues encouraged him to "lie down and put on oxygen" in response to his complaints of a severe headache. Tr. 99-100. Although petitioner treated himself with nasal cannula of oxygen, this did not alleviate his headache symptoms. Tr. 100. Petitioner returned home from his shift at 7:00 a.m. Tuesday morning, November 10, 2009. Petitioner does not recall any events from after he returned home or leading up to his hospitalization later that day. Id.

Mrs. Means testified that she did not notice anything unusual about Mr. Means on Tuesday morning, November 10, 2009, as she only saw him in passing when she was leaving their home to go to work. Tr. 16. When she returned around 3:00 p.m. in the afternoon, she put their one-year old child down for a nap and sat in the living room. Id. She assumed Mr. Means was sleeping, as this was his usual routine, so she minimized any disturbances. Id. Mrs. Means testified that on this afternoon, Mr. Means' behavior was dramatically unusual, in that:

> [he] would get up and come storming into the living room cussing, which was very out of character, very unusual for him. [He] was cussing, was yelling, was angry, was telling me why was I being so loud, what is all the noise for, I can't take it, you've got to stop. And then would go back in [their] room, and he would be curled up in a ball rocking back and forth holding his head. 'I can't take it anymore. I can't take it. It's just got to end. It's just got to stop. I can't do this anymore.' And then two seconds later, he'd be quiet like he was sleeping. And … then it would start all over again. He'd come back out yelling and cussing and

> going on about so much noise. [However,] I wasn't making any noise. The baby was sleeping, and I was sitting at the kitchen table reading a book.

Id.

Mrs. Means testified that this cycle progressively worsened. Tr. 17. Around 6:30 p.m., she called Dr. Cone's office to ask whether the MRI results revealed any abnormalities, but they replied that it had not. Id. Mrs. Means was then instructed to obtain Stadol pain medication from the nearest pharmacy. Tr. 17-18. She left with their baby for the pharmacy and while there received a telephone call from Mr. Means's father inquiring as to his son's well-being. Tr. 18. Mr. Means testified that he apparently called his father while his wife was away, a fact Mr. Means does not recall but was later told by his father. Tr. 76. Mr. Means also testified that his father told him that when he arrived at his son's home that night, Mr. Means did not know how to unlock the dead bolt on the front door and that it took him a long time to comprehend what was being asked of him. Tr. 76-77.

Mrs. Means testified that when she got home from the pharmacy with the medication, petitioner's parents were there. Tr. 18. She stated that at that point, petitioner recognized his father, but he did not recognize her or his mother. Id. He could not tolerate any sound or light, and he was still swearing, crying, rocking, and holding his head. Id. They decided to take him to the ED, but he could not walk down the stairs to get into the car, so they called an ambulance. Id. The paramedics that arrived recognized petitioner from his work at the ED, however, he did not recognize his colleagues. Tr. 19. The paramedics used a lift chair to move petitioner from his upstairs bedroom to the ambulance. Tr. 20.

Petitioner was then transported to the St. Francis Hospital ED. Mrs. Means described petitioner's behavior at the hospital as "very combative, very aggressive, angry, irritated, very disoriented, confused," and he did not recognize his co-workers. Tr. 20. Mrs. Means testified that prior to this episode, petitioner "was a very friendly guy." Tr. 19. "He never met a stranger" and "knew everybody." Id. He was admitted to St. Francis Hospital on Tuesday, November 10, 2009. See Ex. 3.

The medical records reveal that petitioner was admitted to the hospital for headache, dizziness, scotoma, seeing flashing lights, nausea, and vomiting. Ex. 3 at 2. The hospitalist noted that the intake examination was incomplete due to petitioner's "combativeness." Id. Petitioner's parents reported to the hospitalist that he had been experiencing these symptoms over the previous five days. Id. at 2, 13. However, as Mrs. Means testified, this report was inaccurate with respect to the fact that petitioner's parents did not visit with their son after Sunday, November 1, and before Tuesday, November 10, and thus would not have been in the position to report a medical history of the five days leading up to his hospitalization on November 10. Tr. 38.

The consulting neurologist at the ED, Dr. Jagdish Sidhpura, incorporated the hospitalist's and Dr. Cone's histories into his own neurology evaluation on November 10, 2009. Ex. 3 at 13. Dr. Sidhpura noted petitioner's CAT scan of the brain was unremarkable. Id. He also noted, although erroneously, that petitioner received a flu vaccine two weeks prior to his

hospitalization. Id.[6] Dr. Sidhpura further noted that petitioner had no history of migraines or seizures and that this episode was very unusual for him. Id. Physical examination revealed "intense photophobia." Id. at 14. A cerebrospinal fluid ("CSF") analysis revealed elevated protein levels. Id. at 15. Dr. Sidhpura diagnosed a "[one] week history of continuous headaches with acute encephalopathy, especially confusion and combative behavior." Id. at 14.

An electroencephalography ("EEG") performed on Wednesday, November 11, 2009, was "grossly abnormal," showing "an acute encephalopathic process, most likely of toxic metabolic etiology." Ex. 2 at 10. An MRI of the brain, performed on November 13, 2009, suggested possible "edema associated with recent trauma, including diffuse axonal injury" in both hemispheres and a large lesion in the splenium of the corpus callosum. Ex. 3 at 23; Tr. 213.

Mr. Means was transferred to the University of Alabama Birmingham Hospital ("UAB") on November 15, 2009. Ex. 2 at 16. The attending neurologist diagnosed probable acute disseminated encephalomyelitis ("ADEM")[7] based on demyelinating white matter lesions visible on the MRI. Ex. 4 at 3. The doctor prescribed an intravenous corticosteroid, called IV-Solu-Medrol. Id. A repeat EEG on November 17, 2009, indicated "a severe encephalopathic process . . . affecting both [brain] hemispheres." Id. at 47. The EEG revealed frontal intermittent rhythmic delta activity ("FIRDA"), which the physician noted "often implies a metabolic or toxic cause, but could also indicate subfrontal lesions." Id. An MRI performed on November 19, 2009, produced limited images due to Mr. Mean's inability to keep still. Id. at 24. The MRI confirmed brain lesions, although the lesions appeared "less conspicuous" compared to prior studies. Id. Lumbar punctures performed on November 17, 2009, and November 20, 2009, revealed that his CSF had elevated protein levels and myelin based proteins. Id. at 47, 49.

Petitioner was discharged from UAB on November 24, 2009, with a diagnosis of ADEM with cognitive and gait impairments. Ex. 4 at 44. The discharge summary noted that petitioner was "profoundly encephalopathic upon presentation," and that he showed "significant clinical improvement after a five day course of IV Solu-Medrol, but that his gait and movements were abnormal and uncoordinated. Id. at 45. He was transitioned to Spain Rehabilitation Center for further physical and occupational therapies. Id. at 46-47. He was prescribed oral steroid medication, as well as Keppra for seizure prevention. Id. at 46.

Mr. Means received therapy at Spain Rehabilitation Center until November, 27, 2009, when he was transferred back to UAB after becoming unresponsive in the shower. Ex. 4 at 50. During his relapse, he was noted to have experienced tonic clonic movements in his left lower extremity, as well as decreased consciousness with a left-preferred gaze. Id. He was also noted to be drooling and experiencing difficulty hearing. Id.; Tr. 80-81. A November 27 MRI of the brain showed worsening periventricular and corpus callosum lesions, consistent with diffuse encephalitis. Ex. 4 at 72. He was started on a seven day course of IV Solu-Medrol, to no avail. Id. at 80. He then completed five days of plasma exchange treatments. Id. He experienced some

[6] In fact, petitioner received a flu vaccination four days prior to his hospitalization and received a Tdap vaccination a day after the flu vaccine, three days prior to hospitalization. See Ex. 1 at 1.

[7] "ADEM is an initial inflammatory, demyelinating event with multifocal neurologic deficits, typically accompanied by encephalopathy." Nelson Textbook of Pediatrics 2079 (19th ed. 2011).

improvement in his condition after the second exchange treatment. Id. Petitioner was discharged from UAB and sent back to Spain Rehabilitation Center on December 17, 2009.

Petitioner completed rehabilitation and was discharged and returned home on January 7, 2010. Ex. 4 at 144-48. Upon discharge, a neuro-psychological evaluation revealed evidence of decreased attention, severe hearing loss in his right ear, problems with fine motor dexterity, and severe global cognitive deficits, including poor memory, poor processing speed, and poor use of language. Id. at 145-46. His treating physicians recommended that he not return to work and that he receive daily supervision. Id. at 146.

On March 25, 2010, Mr. Means began treatment with a neurologist, Dr. John Rinker. Ex. 4 at 188. Based on a history provided by Mr. Means and his wife, Dr. Rinker recorded that on November 1, 2009, Mr. Means experienced an unrelenting and atypical headache. Id. Dr. Rinker further noted, "About a week later, [Mr. Means] had his regular seasonal flu vaccination," and about three days later, due to persistent headaches, he obtained a routine MRI. Id.

Concerning Mr. Means' condition at that time, Dr. Rinker noted that Mr. Means was "quite a bit better," and he was able to walk, although he had some ongoing balance and coordination difficulties. Ex. 4 at 188. He also noted that Mr. Means continued to have hearing loss and cognitive difficulties. Id. At the time, Dr. Rinker believed Mr. Means experienced "an episode of ADEM," however, he later opined that "the ADEM label was an incorrect diagnosis" in light of petitioner's subsequent diagnosis of Susac's Syndrome. Tr. 132. In March 2010, Dr. Rinker recommended that petitioner continue physical and occupational therapies, and to refrain from resuming work. Ex. 4 at 190.

Mrs. Means testified that petitioner's mobility, balance and coordination was poor in the months following his release from the hospital. Tr. 28. She further testified that petitioner was forgetful and would get confused over simple daily activities, such as getting dressed, showering and brushing his teeth. Id. He would easily become "very angry" and lacked self-control in "dealing with everyday life." Tr. 28, 31. She testified that "his mentality seemed like he reverted to . . . a ten-or-[twelve] year old." Tr. 28-29. According to Mrs. Means, petitioner was in speech, physical and occupational therapies three to four days per week, and his physical and speech therapies continued over the next two years. Tr. 30; see also Ex. 5, 13.

A neuro-psychological evaluation on April 26, 2010, noted, "[W]hile Mr. Means show[ed] a lack of improvement in some areas of neuropsychological functioning, he [had] improved significantly in his daily functioning." Ex. 4 at 213. "His stable performance across two months in some areas suggest[ed] that the prognosis for further improvement [was] guarded, and he may continue to experience residual deficits in processing speed, memory, and executive function." Id. The evaluation further noted that his reasoning skills were variable. Id.

Mr. Means had a follow-up evaluation with Dr. Rinker on May 27, 2010. Dr. Rinker noted that Mr. Means had tapered off prednisone since his March 2010 visit and that his condition had since stabilized, although his hearing continued to suffer. Ex. 4 at 191. Petitioner's May 2010 MRI showed improvement with residual atrophy. Id. at 193. Dr. Benjamin McGrew, an otolaryngologist, fitted Mr. Means with a hearing aid in August 2010 and anticipated that his

hearing would continue to improve "if his demyelination process improves." Id. at 226.

On November 11, 2010, Mr. Means visited Dr. Rinker "on an urgent basis for follow-up of presumed ADEM." Ex. 14-3 at 23. Mr. Means reported that "a little over a week" prior, he began having a new onset headache, increasing somnolence, and had been sleeping for days at a time. Id. By way of a telephone communication the week prior to his visit, Dr. Cone prescribed Prednisone for petitioner's headache. Ex. 12 at 1. Mr. Means reported that the prednisone afforded him some relief but that he was also experiencing some vision difficulties in both eyes. Ex. 14-3 at 23. Dr. Rinker believed petitioner was experiencing new neurological symptoms; particularly optic neuritis in his right eye and possibly an increase in gait ataxia.[8] Id. at 24. He noted that petitioner's disease "could be [evolving] into a different demyelinating condition, such as recurrent ADEM or more atypically, … neuromyelitis optica, or Susac's Syndrome." Id. Upon review of petitioner's November 2010 MRIs, Dr. Rinker noted new areas of abnormality. Id.

Several days after his visit with Dr. Rinker, petitioner was hospitalized for worsening symptoms. Ex. 14-3 at 24. A subsequent ophthalmological evaluation revealed retinal artery occlusions. Id. As a result, he was diagnosed with Susac's Syndrome, based on the triad of encephalopathy, hearing loss, and retinal artery occlusions. Id. Mr. Means was initially treated with daily immunosuppressants, CellCept and Prednisone; however, when that course of treatment failed, he was then started on six cycles of a chemotherapeutic agent, cyclophosphamide. Ex. 10 at 3. Mr. Means responded well to this therapy, and presently, his condition has been largely stabilized, although he continues to have severe deficits in hearing, balance, memory, reasoning, and emotional maturity. Id.; Tr. 32, 172.

As a preliminary matter, the undersigned notes that petitioner aptly testified concerning the events leading up to his vaccinations and the onset of his symptoms, despite the fact that due to his health condition, his memory failed him with regard to the immediate events after receipt of the vaccines. Moreover, Mrs. Means provided credible testimony as to critical events in the days before and after petitioner's vaccinations. As such, the undersigned fully credits their testimony, particularly when corroborated by the contemporaneous medical records.

B. Susac's Syndrome

Susac's Syndrome ("SS") is a condition diagnosed in patients who experience an identifiable triad of symptoms: an encephalopathy, branch retinal artery occlusion ("BRAO"), and hearing loss ("HL"). Ex. E at 86.[9] This condition is an autoimmune endotheliopathy,[10] usually affecting young women ages twenty to forty. Id. SS was first reported by Dr. John O. Susac in 1979, when he treated two women who presented with encephalopathic symptoms,

[8] Ataxia is a "failure of muscular coordination; irregularity of muscular action." Dorland's Illustrated Medical Dictionary 170 (32d ed. 2012) [hereinafter "Dorlands"].

[9] Some of the referenced documents are not numbered. In those cases, the undersigned references the PDF page number.

[10] A pathology affecting the blood vessels. See Dorlands, supra note 8, at 621.

vision loss, and hearing loss caused by small strokes in the brain, retina and cochlea. Ex. 20 at 1. As of 2010, there have been over 200 cases reported. Ex. E at 86. An article published by Dr. Robert Rennebohm and Dr. Susac,[11] among others, notes:

> When only the encephalopathy is present—or when the other [two] components of the triad are not recognized—some clinicians fail to consider SS. Instead, a mistaken diagnosis of multiple sclerosis ("MS") or acute disseminated encephalomyelitis ("ADEM") is made and the patients are treated with a relatively brief course of corticosteroids. Initial improvement may seemingly re-enforce the misdiagnosis, but relapse occurs when corticosteroids are tapered or stopped.

Id.

According to respondent's expert, Dr. Subramaniam Sriram, since the initial discovery of the disease in 1979, the triad of symptoms necessary to make the diagnosis has evolved to a tetrad, and evidence of MRI abnormalities in the corpus callosum of the brain is used to confirm the diagnosis. Tr. 193. The Rennebohm and Susac article notes, "In the encephalopathic form of SS, the corpus callosum is always involved. Usually, callosal microinfarctions are the predominant findings . . . ." Ex. E at 86. Rennebohm and Susac assert that the "diagnosis of SS can be made with certainty in an encephalopathic patient when the [] pathognomonic corpus callosal findings are present, even in the absence of BRAO and HL . . . ." Id. at 87.

Rennebohm and Susac also note:

> It is important to distinguish between the 'encephalopathic form of SS' and the 'recurrent BRAO subset.' The encephalopathic form is characterized by the predominance of encephalopathy at the time of diagnosis, or at the time of peak disease severity. BRAO, hearing loss, or both, may precede, accompany, or follow the encephalopathy, but it is the encephalopathy that dominates the clinical picture and dictates the treatment needs. The encephalopathic form is the most well-known and probably accounts for the majority of definite cases of SS.

Id. at 89. The BRAO subset of SS is characterized by a less severe and prolonged course of recurrent episodes of active retinal vasculopathy, with "symptomatic BRAO at one end of the spectrum and asymptomatic [arteriolar wall hyperfluorescence] at the other." Id. at 89-90.

Dr. Sriram, and petitioner's expert, Dr. Rinker, both agree that information regarding the pathogenesis and natural history of the disease is lacking. Tr. 124, 193. Indeed, Rennebohm and Susac state, "Much remains to be learned about the immunopathogenesis, natural history, clinical characteristics, optimal treatment, and ultimate outcome of SS." Ex. E at 91. However, there is a working consensus that the disease is immune-mediated, as patients respond well to immunosuppressive treatment. Id.; see also Tr. 121-22, 191.

[11] Robert Rennebohm, John O. Susac, Robert A. Egan, & Robert B. Daroff, Susac's Syndrome – Update 299 J. of Neuro. Sci. 86 (2010).

III. EXPERT CREDENTIALS

A. Petitioner's Expert, Dr. John Rinker II

Petitioner's treating neurologist, Dr. John Rinker II, testified on petitioner's behalf as an expert witness. Dr. Rinker obtained his undergraduate degree from Wake Forest University and his medical degree from the Medical College of Georgia. Tr. 106. He completed his internship and residency training in the field of neurology at Washington University in St. Louis. Id. He followed his residency training with a two-year fellowship in both neuro-immunology and multiple sclerosis at Washington University. Id. In addition to his clinical practice as a neuro-immunologist at the University of Alabama at Birmingham Hospital, Birmingham Virginia Medical Center, and Cooper Green Hospital, he is an Associate Professor of Neurology at the University of Alabama, Birmingham. Id.; Ex. 9 at 48. He treats patients with a variety of neuro-immunological disorders, including two patients with Susac's Syndrome (petitioner included). Tr. 123; Ex. 9 at 51.

B. Respondent's Expert, Dr. Subramaniam Sriram

Dr. Subramaniam Sriram is a professor of neurology and microbiology immunology at Vanderbilt Medical Center, where he has been on the faculty for approximately eighteen years. Ex. B at 1; Tr. at 184. He obtained both his undergraduate and medical degrees from the University of Madras in Madras, India. Ex. B at 1. He completed his internship and residency in internal medicine at Wayne State University, followed by a residency in neurology at Stanford University. Id. He also completed a post-doctoral fellowship at Stanford University in neuro-immunology. Id. He is board certified in internal medicine, neurology and psychiatry. Id. He is the associate editor of the Journal of Immunology and has served as a reviewer of several neurology and immunology journals. Tr. 184. In 2009, he co-authored an article[12] concerning a series of patients with Susac's Syndrome treated at the Vanderbilt Medical Center. See generally Ex. D. Along with his teaching responsibilities at Vanderbilt Medical Center, Dr. Sriram also directs its Multiple Sclerosis Clinic. Tr. 185.

IV. STANDARDS FOR ADJUDICATION

The Vaccine Act was established to compensate vaccine-related injuries and deaths. § 300aa-10(a). "Congress designed the Vaccine Program to supplement the state law civil tort system as a simple, fair and expeditious means for compensating vaccine-related injured persons. The Program was established to award 'vaccine-injured persons quickly, easily, and with certainty and generosity.'" Rooks v. Sec'y of Health & Human Servs., 35 Fed. Cl. 1, 7 (1996) (quoting H.R. Rep. No. 908 at 3, reprinted in 1986 U.S.C.C.A.N. at 6287, 6344)).

A petitioner's burden of proof is by a preponderance of the evidence. § 300aa-13(a)(1). The preponderance standard requires a petitioner to demonstrate that it is more likely than not that the vaccine at issue caused the injury. Moberly v. Sec'y of Health & Human Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010). Proof of medical certainty is not required. Bunting v. Sec'y

[12] See Siddharama Pawate et al., The Spectrum of Susac's Syndrome, 30 Neurol. Sci. 59-64 (2009) [Ex. D].

of Health & Human Servs., 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, petitioners must prove that that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." Moberly, 592 F.3d at 1321 (quoting Shyface v. Sec'y of Health & Human Servs., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)); Pafford v. Sec'y of Health & Human Servs., 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner who satisfies this burden is entitled to compensation unless respondent can prove, by a preponderance of the evidence, that the vaccine's injury is "due to factors unrelated to the administration of the vaccine." § 300aa-13(a)(1)(B).

V. EXPERT OPINION AND CAUSATION ANALYSIS

A. Issue

The issue to be resolved is "whether the influenza or Tdap vaccine[s] that the petitioner received on [November 6, and November 7, 2009], substantially contributed to a significant aggravation of a pre-existing injury." See Am. J. Prehearing Sub. at 2.[13]

B. Legal Framework

To receive compensation under the Program, petitioner must prove one of the following: (1) that he suffered a "Table Injury"—i.e., an injury listed on the Vaccine Injury Table within the requisite time period—corresponding to a vaccine that he received, (2) that he suffered an injury that was actually caused by one or both of the vaccines he received, or (3) that he suffered significant aggravation of a preexisting illness as a result of a one or both of the vaccines. See 42 U.S.C. §§ 300aa-13(a)(1)(A) and 11(c)(1). Petitioner must show that a vaccine was "not only a but-for cause of the injury but also a substantial factor in bringing about the injury." Moberly v. Sec'y of Health & Human Servs., 592 F.3d 1315, 1321 (Fed. Cir. 2010) (quoting Shyface v. Sec'y of Health & Human Servs., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)). If a petitioner alleges an injury that is not listed on the Table, the vaccine claim is deemed a non-Table case, and there is no presumption of causation. Rather, as in this case, a claim alleging significant aggravation must satisfy the burden of proof described in Loving, 86 Fed. Cl. at 144.

To establish that a condition was significantly aggravated by a covered vaccine, petitioner must establish, by preponderant evidence:

> (1) the person's condition prior to administration of the vaccine, (2) the person's current condition (or the condition following the vaccination if that is also pertinent), (3) whether the person's current condition constitutes a significant aggravation of his condition prior to vaccination, (4) a medical theory causally connecting such a significantly worsened condition to the vaccination, (5) a logical sequence of cause and effect showing that the vaccination was the reason for the significant aggravation, and (6) a showing of a proximate temporal relationship between the vaccination and the significant aggravation

[13] Petitioner has proven significant aggravation, thus it is dispositive of the issue of whether the Tdap vaccine caused petitioner to suffer a Table encephalopathy within seventy-two hours of vaccination. Accordingly, that issue will not be addressed.

Id. (internal quotations omitted).

The causation theory must relate to the injury alleged. Thus, petitioner must provide a reputable medical or scientific explanation that pertains specifically to this case, although the explanation need only be "legally probable, not medically or scientifically certain." Knudsen v. Sec'y of Health & Human Servs., 35 F.3d 543, 548-49 (Fed. Cir. 1994). Petitioner cannot establish entitlement to compensation based solely on his assertions. Rather, a vaccine claim must be supported either by medical records or by the opinion of a medical doctor. § 300aa-13(a)(1). In determining whether petitioner is entitled to compensation, the undersigned shall consider all material contained in the record, § 300aa-13(b)(1), including "any . . . conclusion, [or] medical judgment . . . which is contained in the record regarding . . . causation." § 300aa-13(b)(1)(A). The undersigned must weigh the submitted evidence and the testimony of the parties' offered experts and rule in petitioner's favor when the evidence weighs in his favor. See Moberly, 592 F.3d at 1325-26 ("Finders of fact are entitled—indeed, expected—to make determinations as to the reliability of the evidence presented to them and, if appropriate, as to the credibility of the persons presenting that evidence"); Althen, 418 F.3d at 1280 ("close calls" are resolved in petitioner's favor).

Another important aspect of the causation-in-fact case law under the Vaccine Act concerns the factors that a special master should consider in evaluating the reliability of expert testimony and other scientific evidence relating to causation issues. In Daubert v. Merrell Dow Pharm., Inc., 509 U.S. 579 (1993), the Supreme Court listed certain factors that federal trial courts should utilize in evaluating proposed expert testimony concerning scientific issues. In Terran v. Sec'y of Health & Human Servs., 195 F.3d 1302, 1316 (Fed. Cir. 1999), the Federal Circuit ruled that it is appropriate for special masters to utilize Daubert's factors as a framework for evaluating the reliability of causation-in-fact theories presented in Program cases.

C. Loving Analysis

(1) Loving Prong One: Petitioner's condition prior to administration of the vaccinations.

The first of the Loving factors requires defining petitioner's condition before he received the vaccinations at issue. The parties agree that petitioner's headache symptoms pre-dated his receipt of the flu and Tdap vaccines on November 6 and 7, 2009, respectively. Am. J. Prehearing Sub. at 1-2. Additionally, both experts agree that petitioner's correct diagnosis is Susac's Syndrome and that a headache can be the first symptom of that condition. Tr. 131-33; 191-94.

Prior to his vaccinations, Mr. Means had an unremarkable medical history and lived an active lifestyle. Petition at ¶ 7. Petitioner's testifying expert and treating neurologist, Dr. Rinker, opined, "In November 2009, Mr. Means was a healthy [twenty-four] year old male, with no known physical, cognitive, or psychiatric problems . . . ." Ex. 16-2 at 2. As a reserve flight medic, Mr. Means regularly engaged in physical activity. Tr. 63-65. When not working in the reserve, he was employed full time as an emergency medical technician at St. Francis Hospital in Columbus, Georgia. Tr. 59.

Petitioner first experienced a headache on the afternoon of Sunday, November 1, 2009, when he worked on a tin roof with his father. Tr. 12-13, 83. Petitioner attributed this headache to not wearing sunglasses to shield his eyes from reflecting rays of sunlight from the tin roof. Tr. 83. When asked to describe his headache, petitioner described it as unremarkable and characterized it as a "twinge of a headache." Id. On November 4, 2009, petitioner arrived at Maxwell Airforce Base with his wife and young child for monthly drill exercises with the Air Force Reserve. Tr. 10-11. Petitioner participated in drill exercises from November 4 through 7, 2009. Id. Petitioner and Mrs. Means testified that petitioner's headache resolved prior to his vaccinations on November 6 and 7, 2009. Tr. 11-12, 88-91 (petitioner testified that he did not experience a headache on November 4 through 6, 2009, and petitioner's wife testified that petitioner did not complain to her of a headache until November 8, 2009). On November 8, 2009, petitioner experienced severe headache symptoms, which he characterized as a "stabbing sensation" that would not "go away." Tr. 94-95. He visited his primary care doctor, Dr. Terry Cone, the next day. Dr. Cone's records from November 9 and 10, 2009, noted that petitioner experienced a "headache since Sunday," and that he presented on November 9 with a severe headache. Ex. 2 at 18, 37. Dr. Cone noted that this headache was ongoing for the previous eight days. Id. at 18.

The undersigned credits petitioner and Mrs. Means' testimony as it suggests petitioner's headache on November 1, 2008, was mild and either resolved or remained mild in the week leading up to his vaccinations. It is unlikely that petitioner would have been able to fully participate in drill exercises November 4-7 if his initial headache was of the same severity as he later experienced following his vaccinations. In the medical record from November 9, 2009, Dr. Cone noted that petitioner felt as though his head would "explode" when he bent down below his chest. Ex. 2 at 37. This is in stark contrast to what petitioner and his wife described as a "twinge" of a headache petitioner experienced on November 1. See Tr. 13, 83. Moreover, petitioner had no other signs or symptoms of illness. Accordingly, the undersigned finds that petitioner's headache on November 1, 2009, either resolved prior to his vaccinations, or that it was mild and did not impair petitioner's ability to participate in reserve drill exercises or activities of daily living.

(2) Loving Prong Two: Petitioner's condition following the vaccinations.

The second Loving factor to discuss is "the person's current condition (or condition following the vaccination if that is also pertinent)." 86 Fed. Cl. at 144. Here, petitioner's condition following his vaccinations is most pertinent.

Petitioner received a flu vaccination on Friday, November 6, 2009, and a Tdap vaccination on Saturday, November 7, 2009. Ex. 1 at 1. Petitioner and Mrs. Means testified that petitioner experienced a severe headache, as well as photophobia, on the evening of Sunday, November 8, 2009. Tr. 18; see also Ex. 2 at 37. When he visited Dr. Cone on Monday afternoon, November 9, 2009, Dr. Cone ordered an MRI of the brain, which was performed on that Monday evening. Id. Ex. 2 at 13. During the examination, petitioner was "really restless and irritable," "agitated" and behaved uncharacteristically in the moments leading up to the study. Tr. 48. The sound and light of the MRI machine aggravated petitioner's headache symptoms. Tr. 49, 98-99. The MRI report noted that part of his study was "technically unreadable because of motion

and/or artifact or both." Ex. 2 at 13. The study was unremarkable and revealed normal results. Id.

At 7:00 p.m. on Monday evening, November 9, 2009, petitioner went to work a twelve hour shift at the St. Francis Hospital ED. While at work he rested in an unused room at the behest of his colleagues due to his unbearable headache. Tr. 99-100. On Tuesday afternoon, November 10, 2009, petitioner came "storming into the living room cussing . . . yelling, [and] angry," and he scolded Mrs. Means for making loud noise. Id. at 16. Petitioner would "then [] go back in [their] room, and would "curl[] up in a ball rocking back and forth holding his head," all the while shouting "'I can't take it anymore. I can't take it. It's just got to end. It's just got to stop. I can't do this anymore.'" Id. Moments later, he would become "quiet like he was sleeping . . . and then it would start all over again. He [would] come back out yelling, [] cussing, and going on about so much noise . . . ." Id.

Petitioner was hospitalized for approximately two months at St. Francis Hospital. He developed severe hearing loss while hospitalized. See Ex. 4 at 146. Dr. Rinker began treating petitioner in March 2010, upon petitioner's discharge from the hospital. Dr. Rinker opined, "The dramatic personality changes, physical disability, and hearing loss which followed [petitioner's] initial hospitalization constitute[d] a dramatic and sustained change from the [petitioner's] baseline functional status." Ex. 16-2 at 2. Dr. Rinker stated, "Following [petitioner's] initial hospitalization, [he] was unfit to return to military service, required cochlear implantation to regain hearing, and has been unable to return to meaningful work." Id. He further stated that petitioner "continues to live with substantial disability. [Petitioner] requires a manual wheelchair for most of his mobility . . . [and] [h]e is a fall risk when standing or attempting to walk." Id.

Petitioner was re-hospitalized in November 2010 with recurring symptoms and newly developed optic neuritis in his right eye. See Ex. 14-3 at 24. An ophthalmological evaluation revealed retinal artery occlusions. Id. Although initially diagnosed with ADEM, petitioner was re-diagnosed with Susac's Syndrome based on his presentation of encephalopathy, hearing loss, and retinal artery occlusions. Id. While petitioner's condition has greatly improved over the last several months, he has not physically or mentally returned to his pre-vaccination state of health. He has diminished hearing which is corrected with the aid of a cochlear device. He currently ambulates in a wheelchair due to his general lack of coordination and inability to balance while standing. Tr. 32-33; Ex. 10 at 2. Ms. Means testified that petitioner's mental state is altered and that he "still has trouble with memory . . . [and] with reasoning, and he'll still get fixated on things." Tr. 32.

(3) Loving Prong Three: Whether petitioner's condition constitutes a "significant aggravation" of his condition prior to the vaccinations.

Concerning whether petitioner's condition constituted a significant aggravation of his Susac's Syndrome, Dr. Rinker acknowledged that some of petitioner's medical records, including his own, noted that petitioner experienced a persistent and unrelenting headache prior to his vaccinations. Tr. 127-30. However, Dr. Rinker opined that dating the onset of petitioner's condition cannot be done with certainty. Tr. 132-33. He posited that if we assume the earliest symptom of the clinical manifestation of his condition was the week prior to his vaccinations, "then the vaccine would certainly prove as an aggravator" based on the testimony and medical

records. Tr. 132-33. Alternatively, according to Dr. Rinker, if the true initiating event of petitioner's disease was the headache symptoms he experienced after his vaccinations, "then the disease itself may have actually begun after the administration of the vaccine[s]." Tr. 133.

Dr. Rinker testified that, with respect to Susac's Syndrome in general, a typical course might be a headache progressing to a personality change, followed by more intense symptoms of encephalopathy. Tr. 131. Additionally, a typical case might involve a headache and encephalopathy, followed by hearing loss or vision loss. Id. Medical literature[14] indicates that partial forms of the syndrome have been reported in a number of patients; "for example, [some patients present with] cochlear and retinal involvement without cerebral symptoms . . . or cerebral and retinal involvement without hearing loss, or retinal involvement only." Ex. 20 at 17.

With regard to petitioner's course of the disease, assuming petitioner already had the beginning of Susac's Syndrome "either in the days leading up to the administration of his vaccines or immediately following it," Dr. Rinker opined that petitioner was experiencing mild symptoms, namely headaches, without cognitive changes. Tr. 132. He further opined that, given the timing of the vaccinations, the fact that Susac's Syndrome is an immune-mediated condition, "and that vaccines by their nature are meant to provoke the immune system into mounting a response . . . [it is] more likely than not the vaccine[s] at least played a triggering role or an exacerbating role in the onset of [petitioner's] disease." Tr. 134.

Respondent's expert, Dr. Sriram, opined that there is no evidence to affirmatively indicate the medical probability that the vaccines in question could significantly aggravate ongoing Susac's Syndrome. Tr. 200. Dr. Sriram based his opinion on the fact that there is no evidence that the Tdap or flu vaccine could worsen an ongoing autoimmune disease. He also pointed out that some vaccines, such as tetanus, can actually reduce the incidence of Multiple Sclerosis. Id. Dr. Sriram noted that there are not very many cases of Susac's Syndrome; however, of the sixteen patients with Susac's Syndrome he currently follows, "about five of them presented with . . . an acute confusional state." Tr. 194. About forty percent of his patients (approximately six patients) "had headache as a first feature" of the disease, due in part to the meninges, which are membranes that envelop the brain. Id. Dr. Sriram further testified that some of his patients with Susac's Syndrome "presented, for example, only with encephalopathy, [and] nothing else—like Mr. Means did" and in those instances, he recommended aggressive treatment from the outset. Tr. 193-94. Dr. Sriram disagreed with Dr. Rinker's testimony that symptoms of Susac's Syndrome can resolve without treatment because, according to Dr. Sriram, "we do not know the natural history of the disease." Tr. 193.

In Dr. Sriram's view, "from the reports of both Dr. Terry Cone who initially saw [petitioner], as well as the emergency room physician . . . [petitioner's headache] was an unrelenting, persisting headache in an otherwise healthy man." Tr. 195. Accordingly, Dr. Sriram

[14] George W. Petty et al., Retinocochleocerebral Vasculopathy, 77 Medicine 12, 18 (1998) [Ex. 20]; see also Gennady Landa et al., Multiple Branch Retinal Arteriolar Occlusions Associated with Smallpox Vaccination, 52 J. of Infection e7, e8 (2005) (noting that a patient with Susac's Syndrome "showed no evidence of sensory hearing loss," a symptom "reportedly exhibited only by two out of three patients with Susac's Syndrome").

believed that the first symptom of petitioner's Susac's Syndrome began on November 1, 2009. Id. at 194.

Dr. Sriram co-authored an article[15] on Susac's Syndrome in which he and his colleagues postulated that "it is not important that all three elements (encephalopathy, retinopathy infarcts, and cochlear infarcts) be present to make the diagnosis" of Susac's Syndrome. Tr. 192. Rather, he recommended that patients receive treatment even when the full "symptom complex has not evolved." Id. According to Dr. Sriram, "There is a very classical, typical pattern of involvement seen in the corpus callosum which makes a physician very suspicious about the diagnosis of Susac's." Tr. 193. The disease has "very particular features" radiologically, which are sufficient to make a diagnosis when one or two elements of the disease are present. Id. This view is echoed in an article co-authored by Dr. Susac providing an update on the nature of Susac's Syndrome. See Ex. E. In that article, the authors "contend that a diagnosis of SS can be made with certainty in an encephalopathic patient when [] pathognomonic corpus callosal findings are present, even in the absence of BRAO and HL." Id. at 87.

Dr. Sriram's article, The Spectrum of Susac's Syndrome, is a report on a series of four patients with Susac's Syndrome. Of the four case reports discussed in the article, "the clinical presentations, [] MRI findings, and [] CSF findings were varied, with long temporal intervals between symptoms, resulting in delay in the fulfillment of the clinical triad in three of the four patients." Ex. D at 59. In the first case, a thirty year old man presented in February 2006 with BRAO in his left eye. Id. "His field loss improved, and in June 2006, [four months later] he suffered superior visual field defect, this time in his right eye. Three days later he experienced an inferior field loss in his left eye along with tinnitus and HL in his right ear." Id. BRAO was noted in both eyes. Id. An MRI of the brain showed widespread lesions and CSF analysis revealed elevated protein. Id. "He was started on oral prednisone 80 mg daily for presumed Susac's syndrome …" Id. at 60. Two weeks later, he developed confusion, short-term memory loss and disinhibition, requiring inpatient hospitalization when his prednisone was reduced. Ex. D. at 60. He was started on an immunosuppressive regimen. Id. Thirty months later, "[h]e continue[d] to do well . . . with no further episodes of BRAO . . . ." Id. at 61. He had "mild permanent visual field defect, normal mentation[,] and no auditory deficits." Id.

Case two of the series, a thirty-four year old woman, presented in 1991 with intermittent vertigo and bilateral hearing loss. Id. at 61. "For the next [ten] years, she continued to have intermittent vertigo and depression and her hearing worsened. In 2001, she developed headaches and lower extremity stiffness." Id. In May and August 2006, she experienced visual difficulties. Id. "[A]n ophthalmologic evaluation . . . showed a visual acuity of 20/70 and the presence of new visual field defects. A presumptive diagnosis of Susac's syndrome was made" and she was treated accordingly. Ex. D. at 6. In December 2007, "[s]he noted improvement in her vision . . . and her visual acuity in the left eye improved to 20/25 and has since stabilized. Immunosuppression was stopped in August 2008." Id.

In case three of the series, a thirty-four year old woman experienced personality changes in 1995. Id. She developed transient diplopia four years later in 1999, along with visual field

[15] See Siddharama Pawate et al., The Spectrum of Susac's Syndrome, 30 Neurol. Sci. 59 (2009) [Ex. D].

defects, headaches, and intermittent numbness in the right arm. Id. "A brain MRI showed non-specific lesions in the corpus callosum" and a CSF study showed elevated protein. Id. Six years later, "[i]n May 2005 she developed sudden bilateral tinnitus and decrease in hearing." Id. In August 2005, "her major problems continued to be psychiatric and cognitive, with difficulties with short-term memory, word-finding, and disorganized thought." Ex. D at 61. A diagnosis of Susac's Syndrome was made two years later, in February 2007, when she had an acute worsening of her vision and bilateral BRAOs were revealed in an ophthalmologic examination. Id. "She was started on a regimen of IVIg . . . and slowly tapered oral corticosteroids." Id. She had another episode of BRAO in September 2007 and was treated with Rituximab and prednisone. Id. "She had no new problems at her last follow-up in March 2008." Id.

In case four of the series, a twenty-five year old woman presented in 1999 with episodes of diplopia and ataxia. Ex. D. at 61. "In 2001 she had an episode of visual blurring, and lost hearing in her right ear." Id. "A diagnosis of Susac's syndrome was entertained [in January 2004], but she did not have any features of encephalopathy, and BRAO was not documented. A brain MRI in March 2005 showed significant involvement of the corpus callosum . . . ." Id. A diagnosis of Susac's Syndrome was made in October 2006 when an ophthalmologic evaluation showed BRAO in the left eye and evidence of old BRAOs in the right eye. Id. at 62. "In September 2007, her central visual acuity dropped to 20/70 right eye and 20/40 left eye and has remained at this level." Id. "A regimen of monthly IVIg was added. At the last follow-up in August 2008, she had no further problems." Id.

Dr. Sriram and his colleagues determined that "the clinical triad may not be apparent for years, resulting in delays in diagnosis." Id. at 59. The authors noted, "[P]resentations with only one, or two, features . . . and delay in the development of the full clinical triad may delay the diagnosis."[16] Id. at 62-63. They stated, "[E]arly diagnosis is key to avoid the development of permanent neurological, visual and auditory deficits." Id. at 59. Additionally, the authors noted that immunosuppressive treatment is effective, however, "[i]t is still not clear how long to treat [] patients with immunosuppression, because symptoms may recur years after remission, and can cause considerable neurological damage in a short time." Id. at 63. They also noted that "there may be long periods of quiescence [or inactivity] even with no treatment," citing a reported case of Susac's Syndrome that recurred after a period of eighteen years. Id. at 63-64.

In the present case, both experts agreed that petitioner's initial ADEM diagnosis was ultimately not the correct diagnosis of his condition. Tr. 132, 195-96. Dr. Rinker believed, "[I]n retrospect . . . the ADEM label was . . . a working diagnosis that was subsequently amended once the . . . full clinical picture was realized." Tr. 132. Dr. Sriram explained, "[T]he MRI is the main differentiating feature" between ADEM and Susac's Syndrome. Tr. 196. Dr. Sriram further explained that in both conditions, a person may experience encephalopathy, seizures, headache, and/or abnormal spinal fluid tests, but that "the picture of what you see in the MRI is what differentiates the acute encephalopathy of Susac's with that of ADEM." Id. Dr. Sriram believed petitioner's correct diagnosis is Susac's Syndrome. Tr. 191.

[16] See also Ex. 20 at 7 (noting "97% of patients did not have the clinical triad at the time of the onset of symptoms. In some patients, the triad became complete after a delay of weeks to more than two years, a factor that contributes to the difficulty in confirming the diagnosis.").

The testimony of both experts and the supporting medical literature reveal that Susac's Syndrome may be characterized by long temporal intervals between the three major features of the disease. See Ex. D at 59; Tr. 131-32, 134, 193-94. The medical literature also shows that some patients manifest symptoms of Susac's Syndrome without positive diagnostic findings to confirm a diagnosis. See Ex. D at 60-62. In petitioner's case, the evidence shows that the course of petitioner's condition was acute and severe, as he developed all three features of the disease (encephalopathy, hearing loss, and vision problems), and positive MRI and CSF findings, within approximately twenty days of his Tdap vaccination on November 7, 2009. See Ex. 3 at 14 (noting elevated protein levels in CSF analysis performed on November 10, 2009); Ex. 2 at 10 (November 11, 2009, EEG showing "an acute encephalopathic process, most likely of toxic metabolic etiology); Ex. 3 at 2 (noting scotoma—a partial loss of vision or a blind spot—and "flashing lights" upon admission to the ED on November 10, 2009); Ex. 3 at 14 (physical examination on November 12, 2009, noting "intense photophobia"); Ex. 3 at 23 (MRI of the brain on November 13, 2009, showing a large lesion in the splenium of the corpus callosum); Tr. 80-81 (noting petitioner had difficulty hearing around November 27, 2009); see also Ex. 4 at 146 (noting severe hearing loss in petitioner's right ear and moderate to severe hearing loss in his left ear).

As both experts acknowledge, not much is known about the natural history of the disease. Nevertheless, the case reports distinguish petitioner's case as more acute, more severe, and with a poorer clinical outcome in comparison. Dr. Sriram's article emphasized intervals of several years to fully manifest the condition, and the only case report in the article that was characterized as a relatively rapid manifestation of Susac's Syndrome took four months to develop. The medical literature also suggests that Susac's Syndrome manifests in partial forms. However, in petitioner's case, the evidence shows petitioner exhibited all three features of the disease in approximately twenty days. As such, the undersigned credits Dr. Rinker's testimony that petitioner was experiencing mild symptoms and would have had a mild course of the disease absent his vaccinations. The evidence also preponderates in favor of petitioner as to both the severity of his condition and the clinical outcome. Compared to the other cases of Susac's Syndrome described in the testimony and the medical literature, petitioner experienced more severe symptoms, requiring hospitalization and lengthy physical and occupational therapies. Petitioner has long-lasting hearing, cognitive, and gait impairments, and he has been unable to return to work. Based on this evidence, petitioner has met his burden of proof to show that his prior condition was significantly aggravated.

(4) Loving Prong Four: A medical theory causally connecting such a significantly worsened condition to the vaccinations.

The fourth Loving factor requires petitioner to put forth a theory causally connecting his significantly worsened condition to the vaccinations. An assessment of whether a proffered theory of causation is reputable must be viewed, "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard . . . ." Andreu v. Sec'y of HHS, 569 F.3d 1367, 1380 (Fed. Cir. 2009). Petitioner is not required to present proof of causation "to the level of scientific certainty," but rather must provide some "indicia of reliability to support the assertion of the expert witness." Moberly v. Sec'y of HHS, 592 F.3d 1315, 1324 (Fed. Cir. 2010). A special master is required to consider all other relevant

medical and scientific evidence contained in the record. Id.; § 300aa-13(b)(1).

Dr. Rinker advances two possible theories for how petitioner's flu and Tdap vaccinations significantly aggravated his Susac's Syndrome. The first theory is molecular mimicry,[17] where antibodies are directed against healthy tissue creating an aberrant immune response. Ex. 16 at 3. "In molecular mimicry, healthy host tissue with some structural similarity to exogenous antigens becomes the target of an immune response directed against the host tissue." Id. Dr. Rinker explained that although he cannot state with certainty that molecular mimicry is precisely what occurred in petitioner's case, the theory explains how an individual's "immune system can go from performing a purely beneficial role to also performing a harmful . . . role in an individual's health." Tr. 136-37.

Dr. Rinker's second theory is that a non-specific immune response was generated in response to the antigens and adjuvants present in the vaccines. Id. at 137. Theoretically, the vaccinations triggered "activation of toll like receptors, uptake and presentation of antigen by dendritic cells, and release of cytokines and chemokines, which signal[ed] upregulation of the host immune system, and which are known to lead to systemic symptoms and non-specific immune activation." Id.

Dr. Rinker based his theories on two considerations. First, that there is an immunological stimulus that occurs fairly soon after the administration of a vaccine. Tr. 118. Dr. Rinker explained:

> [W]hen an individual receives a vaccination, the first immunological responses to the vaccine [are] generated by the innate immune system, which is kind of a nonspecific branch of the immune system. And part of the role of the innate immune system is to react to any novel outside antigen or foreign protein matter and to try to eradicate it in a very nonspecific way … I think most people who've had a vaccination and ever experienced [] muscle aches and flu-like symptoms in the day or days immediately following the vaccine are familiar with the effects on the innate immune system that result when somebody receives a vaccination.

Tr. 117-18. Dr. Rinker further explained that in the process of an innate immune response, an adaptive immune response is stimulated, "which is a more specific and targeted immune

[17] The Institute of Medicine defines molecular mimicry as:

> [S]equence or conformational homology between an exogenous agent (foreign antigen) and self-antigen leading to the development of tissue damage and clinical disease from antibodies and T cells directed initially against the exogenous agent that also react against self-antigen. Molecular mimicry as a mechanism that can cause pathologic damage and disease has been demonstrated in several animal models, most notably experimental allergic encephalomyelitis (EAE) in mice and rabbits.

Institute of Medicine, Adverse Effects of Vaccines: Evidence and Causality 70 (2012) (internal citations removed).

response that takes more time to develop." Id. at 117.

The second consideration on which Dr. Rinker based his proffered theories is the likelihood of an adaptive immune response in a few days following a vaccination. Id. at 118. Dr. Rinker stated:

> [W]hen someone [has] been exposed to a vaccine for the first time, it can take [] upwards of a couple of weeks before the full innate immune response occurs. But when someone has already been exposed to a certain infection or vaccine, the secondary, or the anamnestic adaptive immune response, is quite a bit shorter, on the order of just a few days.

Id. Dr. Rinker relied on a chapter on vaccine immunology written by Claire-Anne Siegrist[18] and a chapter from an Institute of Medicine ("IOM") publication[19] on the adverse effects of vaccines to support his contention that an adaptive immune response can form in a few days after a subsequent exposure to a given vaccine. Dr. Siegrist stated, "In secondary immune responses, booster exposure to an antigen reactivates immune memory and results in a rapid (<7 days) increase of IgG antibody titer." Ex. 23 at 7. The IOM publication indicates:

> Due to the development of memory B and T cells during the primary immune response, the latency between subsequent exposure to the antigen and development of the immune response will usually be shorter. The lag phase [the initial activation of B and T cells] is generally 1 to 3 days; the logarithmic phase [an increase in serum antibody levels] of the secondary antibody response occurs over the next 3 to 5 days.

Ex. 24 at 3. The IOM publication further notes, "While this discussion is not specific to a particular antigen, it can be used as a reference point for the latency between antigen exposure and the initiation of [] immune-mediated mechanisms . . . ." Id.

Dr. Rinker testified that since petitioner received a Tdap vaccination on several occasions in his childhood, a vaccination in 2009 would trigger an "anamnestic adaptive immune response."[20] Tr. 118; see Ex. 1A at 1 (indicating petitioner received "Dtp" or "Dtap" vaccinations on October 1, 1985, November 26, 1985, January 23, 1986, May 9, 1987, June 20, 1990, and July 7, 1990). He further testified that Susac's Syndrome is an immune-mediated condition, likely autoimmune. Tr. 122.

Respondent's expert concedes that Susac's Syndrome is an immune-mediated disease. In

[18] Claire-Anne Siegrist, Vaccine Immunology (2012) in Stanley A. Plotkin et al., Vaccines (6th ed. 2013).

[19] Institute of Medicine, supra note 17, at 70.

[20] "[T]he rapid reappearance of antibody in the blood following the administration of an antigen to which the subject had previously developed a primary immune response." The Sloane-Dorland Annotated Medical-Legal Dictionary 614 (1st ed. 1987).

detail, Dr. Sriram opined, "Although the nature of the immune response in Susac's disease is not known, the response of patients to plasma exchange and more recently reports of remission following depletion of B lymphocytes with Rituxamab would suggest a role for antibodies as a cause for the disease." Ex. A at 4. Dr. Sriram agreed that the prevailing opinion is that Susac's Syndrome may be "antibody mediated," or in other words, be an immune-mediated disease, "for the simple reason [] that the kind of drugs [used] to treat the disease is [sic] best served by those that decrease the antibody levels, or the B lymphocyte . . . ." Tr. 197; accord Ex. 20 at 27 (noting that "[t]he etiology of the disease is unknown, but histopathologic and laboratory evidence suggests that an immune-mediated mechanism may be involved.").

Dr. Sriram agreed that petitioner was correctly diagnosed with Susac's Syndrome, but he opined that petitioner's condition likely began on November 1, 2009, based on the medical records. Tr. 191, 195. He further opined that there is no evidence, "as clinicians," to suggest that vaccinations or any other infection would worsen Susac's Syndrome. Tr. 198. First, according to Dr. Sriram, "[I]f we assume that [petitioner's course] is an amplification of an immune response, then we should have this Susac's . . . exacerbated not only by vaccines, but also by any other exposure to any other infection because . . . [t]he biology of the immune response is the same." Id. "Secondly, if we [] assume . . . that antibodies are related to Susac's, then we have to have a situation or a process by which an infection and/or a vaccine … somehow amplifies the antibody production in the lymph nodes, in the spleen, and targeting them to the end organs to amplify and accentuate the damage." Tr. 189-99. Dr. Sriram testified, "[W]e have no evidence that [] exposure to these antigens, viruses or the vaccines do that . . . ." Tr. 199. For those reasons, Dr. Sriram felt it was "unlikely that [Dr. Rinker's theories] are plausible [] mechanisms . . . ." Tr. 199.

Furthermore, Dr. Sriram stated that he is not aware of any epidemiological or animal studies that have concluded that the vaccines in question can cause or exacerbate Susac's Syndrome. Id. According to Dr. Sriram, the only case report of a possible connection between a vaccination and Susac's Syndrome, submitted by petitioner, is "of a gentlemen who developed another branch retinal artery occlusion after receiving a small pox vaccination. This gentlemen already had Susasc's because his other eye was already affected by a previous branch retinal artery occlusion." Id. As such, Dr. Sriram opined that it is "difficult to conclude that what followed was not otherwise [what] would have happened because that's the nature . . . of Susac's." Id.

The undersigned finds petitioner has provided preponderant evidence to establish a medical theory causally connecting his significantly worsened condition to his vaccinations. Both experts agree that Susac's Syndrome is an immune-mediated disease, likely caused by a dysregulation of antibodies in an immune response. Both experts provided testimony, and the medical literature supports, the proven effectiveness of immunosuppressive therapies in the treatment of this condition, which further supports both the expert opinions that Susac's Syndrome is an immune-mediated condition. See Ex. D at 63-64; Ex. E at 91. Accordingly, petitioner's theory of an aberrant adaptive immune response triggered by the vaccinations at issue, whereby an innate immune response began upon receipt of a flu vaccination on November 6, followed by an anamnestic immune response upon receipt of a Tdap vaccine the next morning, is supported by reliable evidence in this case.

(5) Loving Prong Five: A logical sequence of cause and effect showing that the vaccinations significantly aggravated the petitioner's condition.

The fifth Loving factor requires petitioner to show a logical sequence of cause and effect of how the vaccinations significantly aggravated his Susac's Syndrome.

Petitioner and Mrs. Means testified that petitioner experienced a mild headache on November 1, 2009. Tr. 13, 83. Thereafter, petitioner participated in drill exercises on November 4 through 7, 2009, and received flu and Tdap vaccinations during that time. Tr. 10-11, 88-91. Petitioner and Mrs. Means further testified that petitioner began to experience an intensified headache, as well as the onset of a new symptom, photophobia, on November 8, 2009. Tr. 18. Petitioner visited his primary care doctor on November 9, 2009, who noted that petitioner had experienced a "headache since Sunday . . . [w]ith photophobia and blurring of vision." Ex. 2 at 37.

Dr. Rinker's opinion is that petitioner's severe headache on November 8, 2009, was related to his Susac's Syndrome and that the vaccines played an "exacerbating role in the onset of his disease" for several reasons. Tr. 127-28, 134. First, according to Dr. Rinker, the timing of petitioner's vaccinations is significant. Tr. 134. Here, petitioner received a flu vaccination two days before he experienced symptoms related to his Susac's Syndrome (on November 6, 2009), and received Tdap vaccination one day before his symptoms (on November 7, 2009). Ex. 1. Second, Dr. Rinker also found it significant that petitioner's condition, Susac's Syndrome, "is an immune-mediated disease." Tr. 134. Lastly, he noted "that vaccines by their nature are meant to provoke the immune system into mounting an immune response." Id. In support of his opinion, Dr. Rinker provided several medical articles discussing an association between various vaccines and certain neuromuscular diseases.[21]

Alternatively, Dr. Rinker opined,"[I]f we take [petitioner's] headache a week before to be the initial symptom, then . . . the vaccine would certainly prove as an aggravator." Tr. 133. According to Dr. Rinker, a headache can be an initial symptom of Susac's Syndrome. However, one cannot establish with certainty that petitioner's condition began with a mild headache on November 1, 2009, especially because "based on the testimony [Dr. Rinker] heard [at the hearing], . . . [t]he headache that really stands apart as being distinctly different is the one that began . . . the day following [petitioner's] Dtap [sic] vaccination." Tr. 127.

The undersigned is persuaded by Dr. Rinker's testimony that petitioner's symptoms on November 8 were distinct from the headache he experienced one week prior. Not only do the medical records from November 9 and 10, 2009, document the severity of petitioner's headache in the days following his vaccinations, they also note the onset of new symptoms associated with petitioner's Susac's Syndrome, photophobia and blurring vision. See Ex. 2 at 18, 37. Additionally, on November 10, 2009, petitioner was assessed at the ED with a scotoma (partial loss of vision), and "flashing light" in his vision. Ex. 3 at 2. While it is not unreasonable to

[21] See e.g., H. Orbach & A. Tanay, Vaccines as a Trigger for Myopathies, 18 Lupus 1213-16 (2009); Joerg-Patrick Stübgen, Neuromuscular Disorders Associated with Hepatitis B Vaccination, 292 J. of Neuro. Sci. 1-4 (2010).

suggest that petitioner's Susac's Syndrome began on November 1, 2009, with a mild headache—as some of the medical records ascribe ongoing headache symptoms since approximately November 1—the testimony and the chain of events, namely petitioner's participation in reserve drill exercises from November 4 through 7, establish that petitioner was experiencing mild symptoms of his condition up until two days after his flu vaccination and a day after his Tdap vaccination. After his vaccinations, petitioner's headache symptoms worsened, and he began to experience new disease symptoms. Accordingly, the undersigned credits Dr. Rinker's testimony that petitioner experienced exacerbated symptoms of Susac's Syndrome beginning on November 8, 2009. The undersigned accepts Dr. Rinker's opinion that petitioner's vaccinations were one substantial factor, among other factors, which contributed to an exacerbation of petitioner's condition.

(6) Loving Prong Six: A proximate temporal relationship between the vaccinations and the significant aggravation.

The last prong in the six-part Loving test is "a showing of a proximate temporal relationship between vaccination and [the] significant aggravation." 86 Fed. Cl. at 144. This prong can be informed by the case law relating to Althen prong three. See 418 F.3d at 1280. To satisfy this requirement, petitioner must provide "preponderant proof that the onset of symptoms occurred within a timeframe for which, given the understanding of the disorder's etiology, it is medically acceptable to infer" that the vaccinations played a triggering role. De Bazan, 539 F.3d 1347, 1352 (Fed. Cir. 2008) (citing Pafford v Sec'y of Health & Human Servs., 451 F.3d 1352, 1358 (Fed. Cir. 2006)).

A major point of contention between the experts is whether vaccinations can trigger an exacerbation of an immune-mediated condition twenty-four to forty-eight hours after vaccination. Here, petitioner received a flu vaccination on Friday, November 6, 2009, and a Tdap vaccination in the morning of Saturday, November 7, 2009. Ex. 1. Dr. Rinker opined that petitioner's Susac's Syndrome was significantly aggravated beginning on November 8, 2009. Tr. 126.

Dr. Sriram disagreed with Dr. Rinker on the likelihood of an adaptive immune response forming within just a few days. Dr. Sriram believed that "the kinetics of an immune response to induce the development of an antibody response . . . makes [sic] [a] temporal relationship to the vaccination unlikely," because in "virtually all animals and human studies" the earliest immune response seen is seven days for IgM antibodies, and two to three weeks for IgG antibodies. Ex. A at 4. Dr. Sriram opined that it is unlikely that an adaptive immune response could occur within forty-eight hours, even in the case of a subsequent exposure to an antigen, because "it takes time for the lymphocytes to become plasma cells; plasma cells to make imunoglobins; imunoglobins to be secreted, to circulate[,] and then go into the target." Tr. 202-03. He thought, "48 hours is too short a time frame for the whole maturation process and development process to happen." Tr. 203. However, he did not cite any support for this argument. Id.

Dr. Rinker provided reliable evidence to show that in a subsequent exposure to the same antigen, an increase of IgG antibody titer can occur in less than seven days. Specifically, the Seigrist chapter on vaccine immunology notes, "In secondary immune responses, booster

exposure to antigen reactivates immune memory and results in a rapid (<7 days) increase of IgG antibody titer." Ex. 23 at 7. Additionally, Dr. Rinker provided an IOM publication which notes that in a subsequent exposure to an antigen, activation of B cells, of which Dr. Sriram attributes a primary role in the pathology of Susac's Syndrome, is generally one to three days. See Ex. 24 at 3; Tr. 197. Petitioner provided his childhood vaccination record, indicating several vaccinations with the components in a Tdap vaccine, namely tetanus, diphtheria, and acellular-pertussis. See Ex. 1A at 1. Dr. Rinker opined that because petitioner received Tdap vaccinations on several prior occasions, his Tdap vaccination on November 7, 2009, triggered an anamnestic adaptive immune response within twenty-four to forty-eight hours of his vaccinations. The Seigrist and IOM publications, as discussed above, both support Dr. Rinker's timeframe.

In this case, the temporal relationship between petitioner's vaccinations and the onset of exacerbated symptoms of Susac's Syndrome is compelling. The facts here are consistent with Dr. Rinker's testimony and the supportive medical literature, indicating that an anamnestic adaptive immune response began twenty-four to forty-eight hours after petitioner's Tdap and flu vaccinations, thereby exacerbating his Susac's Syndrome. Assuming, as Dr. Rinker suggests, that petitioner's symptoms of severe headache and photophobia on November 8, 2009, were the start of an exacerbation of his Susac's Syndrome, the evidence supports petitioner's significant aggravation claim. The same holds true if the undersigned accepts Dr. Sriram's contention that petitioner's Susac's Syndrome began on November 1, 2009, as the evidence still supports Dr. Rinker's contention that petitioner experienced an exacerbation beginning on November 8. Accordingly, petitioner has provided preponderant evidence to support a temporal relationship between his vaccinations and his significantly aggravated condition.

VI. CONCLUSION

For the reasons discussed above, the undersigned finds that petitioner has established entitlement to compensation on his claim of a significant aggravation of Susac's Syndrome. Accordingly, petitioner's Table claim will not be reached.

A damages order will be issued separately.

IT IS SO ORDERED.

s/ Nora Beth Dorsey
Nora Beth Dorsey
Chief Special Master